01 November 2001

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 00D-1543
21 CFR Part 11:
Glossary of Terms

My thoughts on the Glossary of Terms Guide, #00D-1543:

Electronic Record

In my opinion, there has been confusion as to exactly what constitutes an electronic record, and when an electronic record becomes official, and subject to the requirements of the rule. The definition also impacts the scope of the rule. I suggest that the following, or similar, additional language be incorporated into the guidance to clarify this definition:

> Electronic record – any combination of text, graphic, data, audio, pictorial, or other information representation in digital form that is created, modified, maintained, archived, retrieved, or distributed by a computer system pursuant to an FDA regulation. The creation of an electronic record is defined as the point at which data are saved and relied upon by the FDA-regulated firm or otherwise used to ensure FDA compliance. In this regard, for manufacturing systems, data are usually relied upon at the time of acquisition and thereafter. Other systems, such a clinical trial reports, are usually relied upon at the time that the report is signed or approved by the authors.
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> [**EXPLANATORY COMMENT**: The guidance does not distinguish which records can be "temporary" and which are not subject to the rule. This seems important. For example, what about the out of specification investigation report -- Is the first draft a "manufacturing record," which has to be subject to an audit trail, or is it a temporary record that does not need to be saved?]

Without this clarification, there is a risk that companies -- or agency officials -- may interpret an electronic record as including temporary records, records in a transient state, those that have not been reviewed and approved, etc. That kind of interpretation could lead to significant unnecessary costs without any corresponding benefit.

Closed System

While the definition of *closed system* as stated in the rule is reasonably clear, some additional clarification might be helpful as to who are the "persons responsible" for the content of electronic records that are on the system. Obviously, it is extremely unlikely that the persons creating the records, such as chemists, operators, or researchers, for example, will also be controlling and managing access to the computer systems. In order to help bring clarity to this definition, may I suggest that the following, or similar, language be added in the guidance document:

> Responsible persons could be from any department within the organization and/or a third party (e.g., independent contractor or other such Agent of the FDA-regulated firm) that is responsible for the content of the records including the Information Technology (IT/IS) staff responsible for maintaining the system. An Agent is anyone who works under a contractual agreement with an FDA-regulated firm or subsidiary organizations.

Open System

While clarifying "responsible persons" in the definition of *closed system* may help this definition, it still could cause confusion in identifying an open system. I suggest the following be added:

> In an open system, data would or could reside for some period of time on a system that is outside the control of the organization that owns the data.

Audit Trail for Electronic Records

The rule discusses audit trails, but does not adequately define the term. The following new definition is suggested:

> Audit Trail for Electronic Records – an automatically generated, accurate, and secure log of each change to an electronic record showing who made the change, what was changed, the reason for the change, and the date and time of the change. The point at which a record becomes an electronic record requiring an audit trail is described in the definition of an *electronic record.*
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> [**EXPLANATORY COMMENT**: We suggest that the words "electronic record" be eliminated from the definition of an audit trail, as this log is to be computer-generated anyway. Also, it is unclear what the terms "secure and non-modifiable" entail. There are very few data that are non-modifiable. Thus, what is needed is an automatically generated log of the changes to e-records.]

Predicate Rule

While the term *predicate rule* is not used in the rule, the application of 21 CFR Part 11 is never the less directly linked to predicate rules. The term *predicate rule* has been used by various agency personnel in talking about the application of Part 11. Because of some confusion that has arisen as to what records must comply with Part 11, a new definition is suggested to be included in the guidance:

> Predicate Rule - A specific regulation (rule) of the Food and Drug Administration, external to Part 11, that establishes a requirement to create, maintain, and archive a particular record or type of record.

I would also suggest that the guidance state that Part 11 is not intended to apply to electronic records or signatures other than those required by predicates rules.

Archive Copy

To help clarify how archiving can be accomplished, I suggest a new definition for *archive copy* be included in the guidance, as follows:

> Archive Copy – an accurate and secure copy of an electronic record that will be retrievable throughout the records retention period required by the predicate rule and will provide a true and accurate representation of the original electronic record. Acceptable means of archiving electronic documents would include electronic technology such as PDF and SAS file formats. An alternative acceptable practice would be printing out a complete copy of the record (original data and all audited changes) and applying a handwritten signature and date.
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> [**EXPLANATORY COMMENT**: We suggest that the bar be set at "accurate" and not "non-modifiable." Also, we suggest adding language to define the "records retention period."]

This will allow the filing of archive documents in durable forms that would be retrievable, and not force firms to maintain old technologies for the sole purpose of accessing archived records.

Data Required by the Predicate Rule

I feel it would be helpful to provide examples of (raw) data required by a predicate rule and, as in the case of the "typewriter exception", examples of "data" to which Part 11 does not apply. It appears to me, the scope of Part 11 is being expanded by FDA inspectors and consultants far beyond data explicitly called for in the predicate rules to what is sometimes referred to as "metadata", an apparently vague and ill-defined term.

For example:

- Data as required by §211.188(b) captured by a manufacturing control system is subject to Part 11.
- The code and system database table structures that are an adjunct, and integral, part of that same manufacturing control system are *not* subject to Part 11.

Raw Data

I suggest that a definition for *raw data* be included in the guidance; for example:

> Raw Data - Any data that are the result of original observations and collection activities necessary for the reconstruction and evaluation of an FDA-required activity or report. Raw data may or may not comprise an electronic record (see the definition for electronic record).
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> [**EXPLANATORY COMMENT**: I suggest the focus should be on FDA-required "electronic" records, not "official records" (which is an undefined term). "Records" can be deleted, as this is covered by "data."]

Metadata

I would really appreciate a definition of "metadata", and I would again find examples extremely helpful too.

For example:

> *Metadata* is composed of those database tables, code or any other support functionality necessary to enable a system to function in order to capture *(raw) data* required by a predicate rule. These structural, supporting components of a system are not explicitly required *data* and therefore are not subject to Part 11.
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> An example would be the underlying structure of the table into which the system places component weights, dates and times and other information required by the predicate rule. Another example would be the code and/or configuration that causes the system to operate in a validateable manner.

Computer System

The rule on electronic records and electronic signatures is directed toward the use of computer systems. Yet *computer system* is not defined in the rule. I suggest the following:

> Computer System – a combination of business process, hardware, software, documentation, and surrounding infrastructure that can be used to capture, create, manipulate, store, or distribute any type of data in digital form. Computer systems do not include simple electronic devices that operate independently of human intervention and do not archive data required by any FDA predicate rule. Examples of such microprocessor-based devices as data loggers, programmable logic controllers (PLCs), temperature control loops, or other chip-based stand-alone controllers or data collectors.
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> [**EXPLANATORY COMMENT**: I feel the description of a computer system should be more robust. Also, I believe the exclusion should be limited to devices that are independent of human operators.]

This will clarify that certain self-contained devices or temporary data storage devices are not electronic records and are not intended for inclusion in the application of Part 11.

Part 11 Compliance Schedule

I believe it would be helpful to add a definition for a *Part 11 compliance schedule.* For example:

> Part 11 Compliance Schedule - a documented schedule or plan which has been developed to assist in the orderly implementation of Part 11 requirements into an organization's FDA-regulated operations. The plan should include timing of the implementation, prioritization of systems by importance/function and should be integrated into the routine capital replacement plan of the organization.

This will allow the other guidances to reference a defined term.

Typewriter Exception

There appears to me to still be confusion about the so-called "typewriter exception", as referred to in the Preamble - item number 22, even though it has been discussed at length.

I do agree that raw data first written, say by a laboratory instrument or a manufacturing control system, to durable media is not excepted from Part 11 even though a paper record may be printed, signed and designated the "official record".

However, I have heard FDA persons, industry consultants and industry members state that document systems are subject to Part 11 in the cases where the ultimate product of that system is a printed, signed and considered by all to be "the" official document. For example, procedures that are created on a PC, then printed, signed and filed as the official document. Or similarly, forms that are filled out electronically, but then are printed, signed and filed as the official documentation that they were designed for.

I believe Section 22 of the Preamble is itself in disagreement with the point of view that a procedure (SOP) created using MS WORD that is printed, signed & filed as the official procedure also creates an electronic record subject to Part 11. I believe that the word-processing system is indeed incidental to the creation of the document.

The document author, by signing the document as the author, is attesting to the fact that the document is as he/she intended. Those who review and approve the document are, among other things, attesting to the fact that the document is as they intend it to be. Any changes, controlled or uncontrolled, audited or un-audited, that happened before the document was printed are irrelevant from the regulatory point of view, in my opinion.

I believe it would be helpful to further clarify this issue by adding the definition and the example in the Preamble to the Glossary and by listing a couple more examples, as follows:

> Typewriter Exception – Part 11 is not intended to apply to computer systems that are merely incidental to the creation of paper records that are subsequently maintained in traditional paper-based systems. In such cases, the computer system would function essentially like manual typewriter and any signatures would be traditional handwritten signatures. Record storage and retrieval would be of the traditional 'file cabinet' variety. More importantly, overall reliability, trustworthiness, and FDA's ability to access the records would derive primarily from well-established and generally accepted procedures and controls for paper records.
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> For example, if a person were to use word processing software to generate a paper submission to FDA, part 11 would not apply to the computer system used to generate the submission, even though, technically speaking, an electronic record was initially created and then printed on paper.
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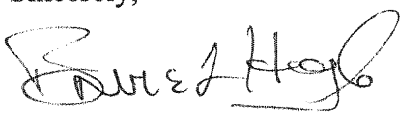
> A second example would be operating procedures that are created electronically, but then are printed, signed, approved and filed as a paper document and are considered to be 'the' official document.
>
> Yet another example would be a form that is filled out electronically, but then is printed, signed, approved and filed as a paper record and is considered to be 'the' official document.

Thank you for the opportunity to comment on the draft guidance. I hope that these comments will be informative and useful as finalization of the guidance proceeds.

Sincerely,



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